

VIII. *The Changes in the Breathing and the Blood at Various High Altitudes.**By* MABEL PUREFOY FITZGERALD.*Communicated by* Dr. J. S. HALDANE, F.R.S.

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In connection with the Anglo-American Pike's Peak Expedition (1911), and simultaneously with the work on the summit of Pike's Peak, Colorado, U.S.A., the following experiments were made in Colorado during the months of July and August, 1911, at altitudes varying from 5000 to 12,500 feet, for the purpose of determining the changes in the alveolar air and in the percentage of hæmoglobin in the blood of persons residing permanently at such heights.

HALDANE and PRIESTLEY* showed that normally the lung ventilation is so regulated as to maintain during rest a definite mean alveolar carbonic acid pressure, and it is known that at high altitudes the breathing is regulated to a lower alveolar CO₂ pressure than is the case at sea-level. It is also known that an increase in the percentage of hæmoglobin occurs with a rise in altitude.†

Until now, the observations on the changes in the alveolar air and hæmoglobin at high altitudes have been practically confined to the various observers and their companions, who were making but a short stay at various heights, and no systematic work has been done on residents, or over a wider range of altitude. For such work Colorado is eminently suitable, as not only are there several readily accessible towns situated at a high altitude, but mines, at which the miners both work and live, are to be found up to the height of 13,000 feet.

There are two records of previous work done on the blood in Colorado: that of CAMPBELL,‡ who, experimenting at heights varying between the foot and the summit of Pike's Peak, found an increase in the blood corpuscles in men and in rabbits; and that of KEMP and his companions,§ who made observations at Champaign, Cripple Creek, and on the summit of Pike's Peak. In the brief report given of this work, KEMP states that both the red corpuscles of the blood and the hæmoglobin increased with rise in altitude, but no parallelism existed between the two; at Cripple Creek the increase in hæmoglobin preceded that of the red corpuscles. He further mentions diurnal fluctuations in both the hæmoglobin and the red corpuscles, the corpuscular count being higher in the morning than in the afternoon. He gives

* 'Journ. Physiol.,' 1905, vol. 32, p. 225.

† Reference to the work and the opinions of the many observers who have directed their attention to the changes in the alveolar air and blood at high altitude has already been made in the preceding paper by DOUGLAS, HALDANE, HENDERSON, and SCHNEIDER. To save repetition, the reader is referred to this and to the work of ZUNTZ, LOEWY, MÜLLER, and CASPARI, 'Höhenklima und Bergwanderungen,' 1906.

‡ Referred to by ZUNTZ and his colleagues, *loc. cit.*, p. 176.

§ "Proceedings of the American Physiological Society," 'Amer. Journ. Physiol.,' vol. 10, p. xxxii.

no estimate of the increase in the hæmoglobin at any point, nor does he mention the method employed in its determination.

The present investigations were made at twelve localities between approximately $38^{\circ} 55'$ and $37^{\circ} 55'$ latitude and 105° and 107° longitude, the distance travelled between Denver—the most northerly and lowest point—and the Lewis Mine, near Telluride—the most southerly and highest—being about 440 miles. The trip, of which a brief description is given, can be divided roughly into four parts: (1) Denver and Colorado Springs, (2) Cripple Creek, (3) Ouray, and (4) Telluride.

Denver (altitude 5100 feet), situated but a few miles from the Rocky Mountains, and Colorado Springs (altitude 6000 feet), on the edge of the foothills, with Pike's Peak as the background, are about 74 miles apart. The Cripple Creek district, an open mountain country, formerly a cattle range, is between 50 and 60 miles by rail from Colorado Springs, and looks out on the west side of Pike's Peak. In this district, Victor (altitude 9850 feet) formed the base, and the places visited from there, the Portland Mine and Mill (altitude 10,090 and 10,300 feet respectively) and Altman (altitude 10,870 feet), were reached by an electric railway or on foot.

The Ouray district, situated in the south-western part of the State, in the midst of very wild, mountainous country, was reached by the Denver and Rio Grande Railway, through the Grand Cañon of the Arkansas River, over the Marshall Pass, crossing the Continental Divide of the Rocky Mountains at a height of 10,856 feet, thence through the Black Cañon of the Gunnison and into the valley of the Uncompahgre River, in which were situated two of the selected centres for work, the towns of Ridgway (altitude 6990 feet) and Ouray (altitude 7780 feet). Ridgway is in an open part of the valley, though in the neighbourhood of Mount Uncompahgre (altitude 14,420 feet). Ouray, 387 miles from Denver, one of the oldest of the Colorado mining camps, is situated in a basin, and, to all appearance, completely walled in by rugged mountain ranges, varying in height from 10,000 to 13,500 feet (Whitehouse Mountain, Hayden Mountain, etc.).

The Camp Bird Mill (altitude 9500 feet), with its colony of miners, shut in at the head of a gulch, was reached from Ouray by mountain "stage." From the mill up to the Camp Bird Mine (altitude 11,300 feet), about 2000 feet above it and a distance of about 2 miles, the journey was made on horseback, while the gas analysis apparatus and other equipment reached the same destination by means of the aerial tramway used for the transportation of ore and the conveyance of supplies to the mine. Round the mine the country is bleak, and Mount Sueffles (altitude 14,158 feet) is close by. The condition of the trail, owing to deep snow, prevented an approach on horseback from the Camp Bird Mine to the high mines in the neighbourhood of Telluride, which place had then to be reached, with loss of valuable time, by the Rio Grande Southern Railway from Ridgway. Observations were made at Telluride (altitude 8770 feet), situated in the St. Miguel Valley amidst very wild and high mountains, and thence at two neighbouring mines, (1) the Tom Boy (altitude

11,500 feet), a few miles to the north-east, accessible by a good wagon road, and (2) the Lewis (altitude 12,500 feet), several miles by trail in another direction, reached on horseback, accompanied by a guide, with the gas analysis apparatus and equipment strapped to our saddles.

The aforementioned towns and mining camps selected for the investigations were chosen with the view that each place should be separated by progressive altitudes of 1000 feet. In the Cripple Creek district observations were made at altitudes which differed only by 300 or 500 feet. Unfortunately, owing to lack of time, it was impossible to obtain the alveolar CO_2 and the hæmoglobin values for altitudes between 1000 and 5000 feet. In the charts accompanying the paper, the supposed values for such heights are indicated by a broken line, and the observed and supposed values for altitudes higher than 14,100 feet are similarly indicated.

The investigations awakened keen interest, and every facility, including good accommodation for work, was afforded. After leaving the Biological Laboratory of Colorado College, this varied from the office of a mining engineer in a "skyscraper" building and the library of the Medical Association at Denver, to a chemical laboratory situated at 10,300 feet in connection with the mill of the Portland Mine; from the well-furnished room of the mine directors to the wooden hut of the miners, the miners' reading and hospital rooms, the substantial town hall of Ouray and the one-storied wooden substitute in a declining mining camp, which still boasts of its position as the highest incorporated town in America (10,780 feet).

Observations were made by me on 131 residents in twelve localities of different altitudes. Observations on the percentage of hæmoglobin in the blood of male residents on the summit of Pike's Peak, made by my colleagues there, are included in the tables and charts; also the mean of the alveolar CO_2 records obtained by my colleagues for themselves during the latter part of their stay on the summit. The results obtained for myself at the different localities visited are given for fourteen different altitudes.

The research is based on 513 alveolar CO_2 determinations and 128 hæmoglobin percentage determinations.

With the exception of seven young men and women, aged between 15 and 19 years, the subjects were adult men and women of from 20 to 70 years of age. The number of subjects corresponding to each decade, or part thereof, were as follows:—

Age.				Number.			
Between	15	and	19 years	.	.	.	7
„	20	„	29	„	.	.	45
„	30	„	39	„	.	.	41
„	40	„	49	„	.	.	21
„	50	„	59	„	.	.	13
„	60	„	69	„	.	.	3
„	70	„	79	„	.	.	1

Several of the subjects had lived at high altitudes from birth, some had never been at a lower level than 5000 feet.

At Colorado Springs, Denver, Ouray, Telluride and Ridgway, the subjects were mainly university students, mining, medical and other professional men and women ; in the gold and silver mining camps above 9000 feet altitude, the subjects were men belonging to the managing and working staffs of the various mines and mills, their wives and female relations.

In the selection of subjects, care was taken to exclude the unhealthy ; also persons who, owing to quite recent arrival at the altitude in question, might not yet be adapted to their new conditions. To ensure adaptation, one year's residence at a high altitude was, as a rule, stipulated for ; and in the case of change of abode within the range of high altitudes, six weeks to two months was usually taken as the minimum time.

For the sake of comparison, four newcomers to high altitudes were included, whose length of residence varied from six weeks to three months : also a few subjects who had spent less than six weeks at a given high altitude. Two subjects, permanent residents at 6000 and *circa* 8000 feet, had returned one and two weeks respectively from a brief stay at sea level ; otherwise no subject had been either at sea level, or at a lower altitude than 5000 feet, for a considerable time. Business transactions caused one or two of the subjects to descend one or two thousand feet once a week, but, generally speaking, a month had elapsed since any subject left, even for a day, the place at which he or she was living.

Haldane's air analysis apparatus* was used for the determinations, and the samples were obtained by the direct method, as described by FITZGERALD and HALDANE.† The indirect method for determining the alveolar CO₂ tension, employed by various Continental observers, appears to give very variable results, owing to the uncertainty caused by the "dead space" of the respiratory passage being taken as a definite volume.‡ With the exception of a few cases, in which it was only possible to obtain "end of expiration" samples, samples were taken at the end of a normal inspiration and at the end of a normal expiration, the mean percentage value for the CO₂ obtained by the analysis of these being taken as the value of the CO₂ in the dry alveolar air. The alveolar CO₂ tension was calculated from the results of the analyses and the readings for the barometric pressure, after allowing for the pressure of aqueous vapour (47 mm. of mercury) in the alveolar air saturated at 37° C. The alveolar oxygen values, given only as mean results for each locality, have been calculated from the mean CO₂ values recorded for the given locality, allowing for 0.03 per cent. CO₂ in the air and assuming that the deficiency of O₂ in the alveolar air is one-fifth greater than the excess of CO₂.

* See p. 48 of HALDANE'S 'Methods of Air Analysis,' London, 1912.

† 'Journ. Physiol.,' 1905, vol. 32, p. 486.

‡ See DOUGLAS and HALDANE, 'Journ. Physiol.,' 1912, vol. 45, p. 235.

If the value for the CO_2 pressure is used for the determination of the O_2 pressure, the calculation is made as follows :—

$$\frac{\text{Excess of } \text{CO}_2}{\text{Deficiency of } \text{O}_2} = \frac{5}{6}.$$

At Oxford, for instance, with a mean barometric pressure of 748 mm. of mercury, the normal mean CO_2 pressure in alveolar air, saturated at 37° , was 39.2 mm. of mercury (men). In inspired air the O_2 pressure = $\frac{20.93}{100} \times 748$, or, allowing for saturation at 37° ,

$$\frac{20.93}{100} \times (748 - 37),$$

i.e. 147 mm. of mercury. Therefore the O_2 pressure in alveolar air = $147 - (39.2 \times \frac{6}{5})$, *i.e.* 100.0 mm. of mercury.

Taking Denver as another example, where the barometric pressure was reduced to a mean value of 625 mm. of mercury and the mean alveolar CO_2 pressure was 35.98 mm. of mercury, the O_2 pressure in inspired air, allowing for saturation at 37° , = $\frac{20.93}{100} \times (625 - 47)$, or 121.0 mm. of mercury. Supposing the partial pressure of CO_2 in the alveolar air had still been 39.2 of mercury, the partial pressure of O_2 in alveolar air would have been $121.0 - (39.2 \times \frac{6}{5})$, *i.e.* 73.9 mm.; but the mean partial pressure of CO_2 in the alveolar air was actually 36.0 mm., therefore the mean pressure of O_2 in the alveolar air was $121.0 - (36.0 \times \frac{6}{5})$, *i.e.* 77.8 mm. of mercury.

A carefully standardised Gowers-Haldane hæmoglobinometer was used for determining the hæmoglobin percentage. At altitudes above 6000 feet, pure CO was used for saturating the blood solution. By this method the sample of blood is compared with a standard solution of blood of known oxygen capacity, saturated with CO. Since, as shown by HALDANE,* the colouring power of the blood varies exactly with its oxygen capacity, the results obtained by using the Gowers-Haldane instrument are not mere arbitrary results, as is the case with other colorimetric methods, based on the use of coloured glass or more or less unstable and indefinite coloured solutions, but afford definite physiological information, as the hæmoglobin can be expressed in terms of its oxygen capacity, the 100 mark on the scale corresponding to 18.5 per cent. oxygen capacity, found by HALDANE and LORRAIN SMITH† to be the mean oxygen capacity of the blood in normal man.

At Denver and Colorado Springs the readings for the barometric pressure were obtained from the meteorological stations there; at other places readings were taken from an aneroid barometer compensated for temperature, and reading to 20,000 feet, and set for Colorado Springs. The readings obtained from the aneroid were checked

* 'Journ. Physiol.,' 1901, vol. 26, p. 497.

† 'Journ. Physiol.,' 1900, vol. 25, p. 342.

against records for the district and by calculations made by a member of the staff of the U.S. Meteorological Office at New York. As they were in close agreement with these findings, the actual readings have been used for the calculations in the present paper. For the Lewis Mine (altitude 12,500 feet) the barometric pressure calculated for altitude is used. On the return to Colorado Springs, readings corresponding closely to the mean barometric pressure recorded for that locality (615 mm. of mercury) were obtained from the aneroid both on the day of arrival and on the two following days, *i.e.* 617 mm. and 614 mm. of mercury.

The altitude of the different localities was taken, in the majority of cases, from the bench marks of the U.S. Geological Survey.

With other particulars Table I gives the mean values for the hæmoglobin percentage, the alveolar CO₂ percentage and pressure, and the calculated alveolar oxygen pressure obtained for men at localities varying in altitude from 5000 to 14,100 feet, and normal mean values for near sea level (Oxford) are included for comparison. Table II gives similar values for women.

When the values for the alveolar CO₂ and O₂ pressures are plotted in conjunction with the observed values for barometric pressure (Chart I), it is seen that with increase of altitude there is a progressive decrease in the alveolar CO₂ pressure, and that this decrease is in linear ratio to the barometric pressure. Taking extreme values it may be said that for every fall of 100 mm. of barometric pressure there is a fall of 4.2 mm. of pressure in the alveolar CO₂. There is likewise a progressive fall in the oxygen pressure.

In Chart I, in addition to the graphs showing the partial pressures of O₂ and CO₂, a curve is plotted showing the values for the barometric pressure when the mean temperature of the air column between sea-level and the heights indicated is assumed to be 15° C. This has been calculated from the following formula quoted by ZUNTZ and his collaborators in 'Höhenklima,' p. 38 :

$$\log b = \log B - \frac{h}{72(256.4 + t)},$$

where B = the barometric pressure at the lowest level,

$b =$ „ „ „ upper level,

$h =$ the difference in height in metres,

$t =$ the mean temperature of a column of air from the height h .

When a mean temperature of 15° is assumed the calculated pressures seem to correspond closely with the pressures observed on high mountains, at least in summer, when the weather below is warm. This is shown in Table III. The barometrical observations were made in summer, and the calculated values are for a mean temperature of 15° C.

Near sea level (Oxford), the alveolar CO₂ values were found to be definitely lower in women than in men, the mean normal CO₂ percentage being 5.17 against 5.59 in

TABLE I.—Mean Results obtained for Men.

Locality.	Altitude.	Mean baro- metric pressure.	CO ₂ .			No. of subjects and of CO ₂ determinations.		O ₂ .	Hæmoglobin.				
			Mean percent- age in dry alveolar air.	Pressure in alveolar air saturated at 37°.		Sub- jects.	Determi- na- tions.		Percentage.		No. of determi- na- tions.		
				Mean.	Max.				Mean.	Min.			
Denver . . .	feet. 5,100	mm. Hg. 625	6.22	mm. Hg. 35.98	mm. Hg. 39.34	9	28	13.51	78.03	114.8	127	110	5
Colorado Springs	6,000	615	5.96	33.85	37.05	8	40	13.82	78.44	108.8	112	106	6
Ridgway . . .	6,990	590	6.10	33.14	36.54	4	12	13.65	74.12	118	118	—	1
Ouray . . .	7,780	573	5.82	30.65	36.03	13	41	13.99	73.53	118.8	134	110	10
Telluride . . .	8,870	550	5.98	30.05	33.35	5	14	13.79	69.86	118.5	121	116	2
Camp Bird Mill	9,500	533	6.15	29.90	34.41	12	40	13.59	66.05	122.6	133	116	7
Portland Mine .	10,090	519	6.25	29.47	32.40	10	38	13.47	63.58	124.4	135	117	9
Portland Mill .	10,300	515	6.45	30.21	32.78	10	31	13.23	61.92	120.8	125	113	10
Altman . . .	10,728	508	6.53	30.06	34.31	9	23	13.13	60.53	—	—	—	—
Camp Bird Mine	11,300	502	6.15	28.00	34.21	22	63	13.61	61.93	126.5	143	116	22
Lewis Mine . .	12,500	480	6.11	26.50	28.90	6	17	13.64	59.15	123.2	134	111	5
Pike's Peak . .	14,100	458	6.58	27.00	30.4	4	16	13.07	53.72	130.8	153	116	16
Oxford. . . .	—	748	5.59	39.2	44.5	27	130	14.26	99.96	100	113	87	(9 subjects) 26

TABLE II.—Mean Results obtained for Women.

Locality.	Altitude.	Mean baro- metric pressure.	CO ₂ .			No. of subjects and of CO ₂ determinations.		O ₂ .		Hæmoglobin.			No. of determina- tions.	
			Mean percent- age in dry al- veolar air.	Pressure in alveolar air saturated at 37°.			Sub- jects.	Determina- tions.	Calculated mean percentage in dry alveolar air.	Calculated mean pressure in alveolar air saturated at 37° C.	Percentage.			
				Mean.	Max.	Min.					Mean.	Max.		Min.
Denver . . .	feet. 5,100	mm. Hg. 625	5.78	mm. Hg. 33.37	mm. Hg. 35.31	29.95	4	12	14.04	82.09	101.8	103	101.5	2
Colorado Springs	6,000	615	5.36	30.45	32.71	27.56	4	19	14.54	82.53	104	106	102	2
Ouray . . .	7,780	573.5	5.17	27.18	31.77	22.72	6	17	14.77	77.79	118.8	130?	110	6
Portland Mine .	10,090	518	6.07	28.57	30.10	27.04	2	7	14.65	64.43	—	—	—	—
Camp Bird Mine	11,300	502	5.70	25.92	27.53	24.30	2	7	14.13	64.29	113.3	114.5	112	2
Tom Boy Mine .	11,500	496	5.72	25.67	28.33	20.74	4	9	14.11	63.31	120	129	103	3
Sea level . . .	—	749*	5.17*	36.3*	41.00	30.4	32*	138*	14.77	103.62	89†	96	81	12

* See FITZGERALD and HALDANE, 'Journ. Physiol.,' 1905, vol. 32, p. 486.

† See HALDANE, 'Journ. Physiol.,' 1901, vol. 26, p. 503.

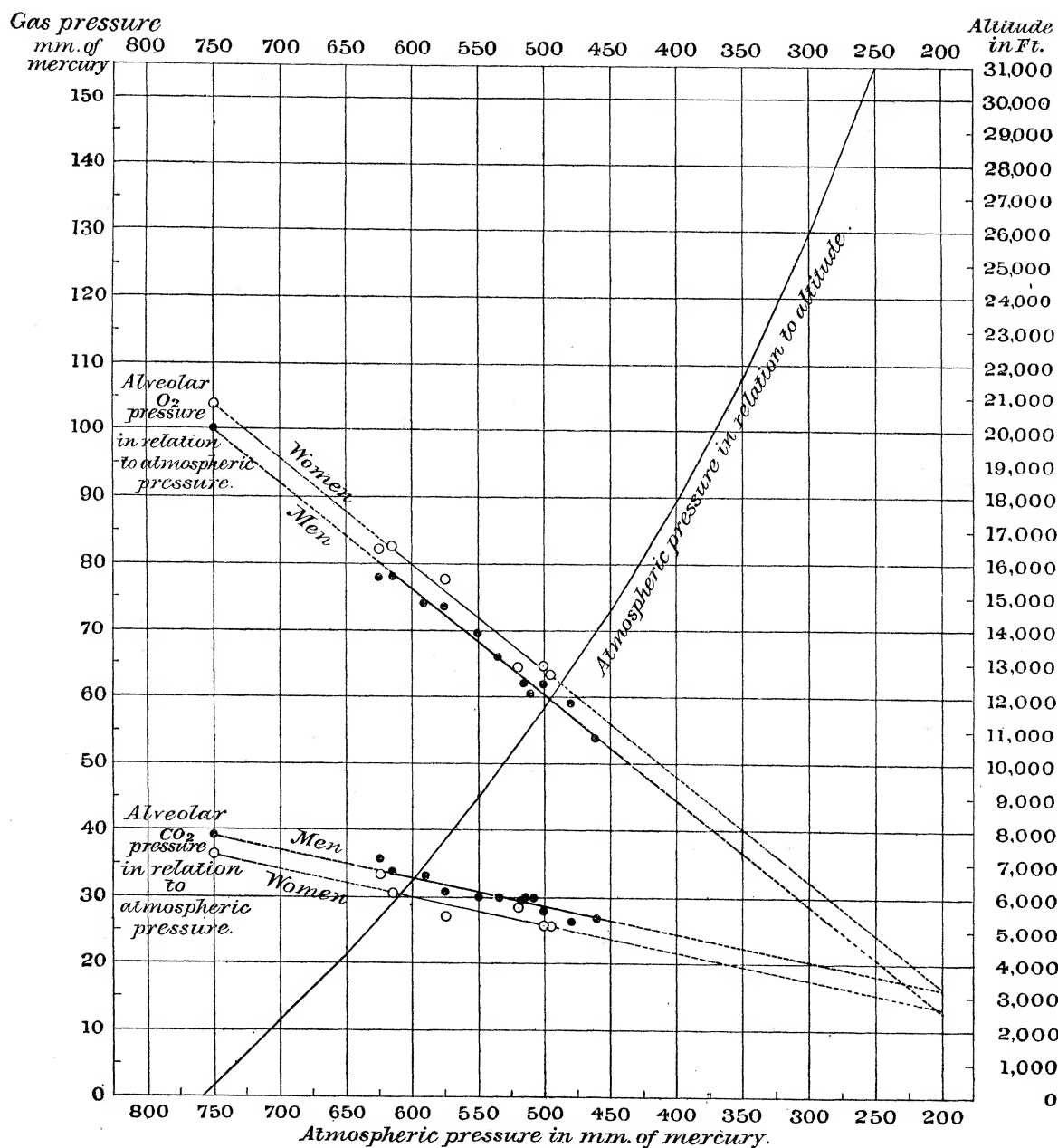


Chart I.

men (barometric pressure 749 mm. of mercury), and the CO₂ pressure 36.3 mm. of mercury against 39.3 mm. in men.* This difference in the physiological constants for the alveolar CO₂ persists also at high altitudes, but it is found that the diminution in the alveolar CO₂ pressure at progressively increased altitudes is relatively the same in men and women, as is seen clearly in Chart I and Tables I and II.

Allowing for the difference in degree of adaptation, the CO₂ pressures recorded for men at Denver, Ridgway, and Altman correspond with the CO₂ pressure values

* FITZGERALD and HALDANE, 'Journ. Physiol.,' 1905, vol. 32, p. 486.

obtained by WARD* and by DOUGLAS† at similar altitudes (Zermatt, 5315 feet ; Las Canadas, 7000 feet ; Alta Vista, 10,700 feet).

TABLE III.

	Altitude.		Atmospheric pressure.	
	Metres.	Feet.	Observed.	Calculated.
Denver	1,554	5,100	625	633
Colorado Springs	1,829	6,000	615	613
Ridgway	2,131	6,990	590	591
Ouray	2,371	7,780	573	575
Telluride	2,704	8,870	550	553
Camp Bird Mill	2,896	9,500	533	540
Portland Mine	3,075	10,090	519	530
Portland Mill	3,139	10,300	515	525
Alta Vista (Teneriffe)	3,261	10,700	519	518
Altman	3,270	10,728	508	516
Camp Bird Mine	3,444	11,300	502	506
Tom Boy Mine	3,505	11,500	496	503
Lewis Mine	3,810	12,500	480	485
Pike's Peak	4,300	14,109	458	458
Monte Rosa	4,560	14,965	440	444
Chimborazo	6,248	20,500	358	362
Himalayas	7,492	24,580	312	314

TABLE IV.

Approximate altitude when mean temperature of air column = 15° C.		Atmospheric pressure.	Alveolar air.			
			Percentage.		Partial pressure.	
Metres.	Feet.		O ₂ .	CO ₂ .	O ₂ .	CO ₂ .
Sea level	Sea level	760	14·33	5·58	102·2	39·8
122	400	750	14·26	5·59	100·0	39·2
698	2,290	700	14·17	6·66	92·9	37·1
1,326	4,350	650	14·01	5·80	84·5	35·0
2,004	6,578	600	13·83	5·95	76·5	32·9
2,743	8,999	550	13·62	6·12	68·5	30·8
3,552	11,653	500	13·36	6·34	60·5	28·7
4,447	14,589	450	13·05	6·60	52·6	26·6
5,445	17,864	400	12·64	6·94	44·6	24·5
6,579	21,584	350	12·10	7·39	36·7	22·4
7,889	25,882	300	11·34	8·02	28·7	20·3
9,437	30,960	250	10·24	8·97	20·8	18·2

On the assumption that the alveolar CO₂ pressure falls continuously with the atmospheric pressure, and taking the fall in CO₂ pressure to be 4·2 mm. for every

* 'Journ. Physiol.,' 1908, vol. 37, p. 378.

† *Ibid.*, 1910, vol. 40, p. 454.

100 mm. fall in atmospheric pressure, values for the alveolar gas percentages and pressures in men have been calculated for atmospheric pressures varying from 760 mm. to 250 mm. of mercury. These are given in Table IV and represented in Chart II.

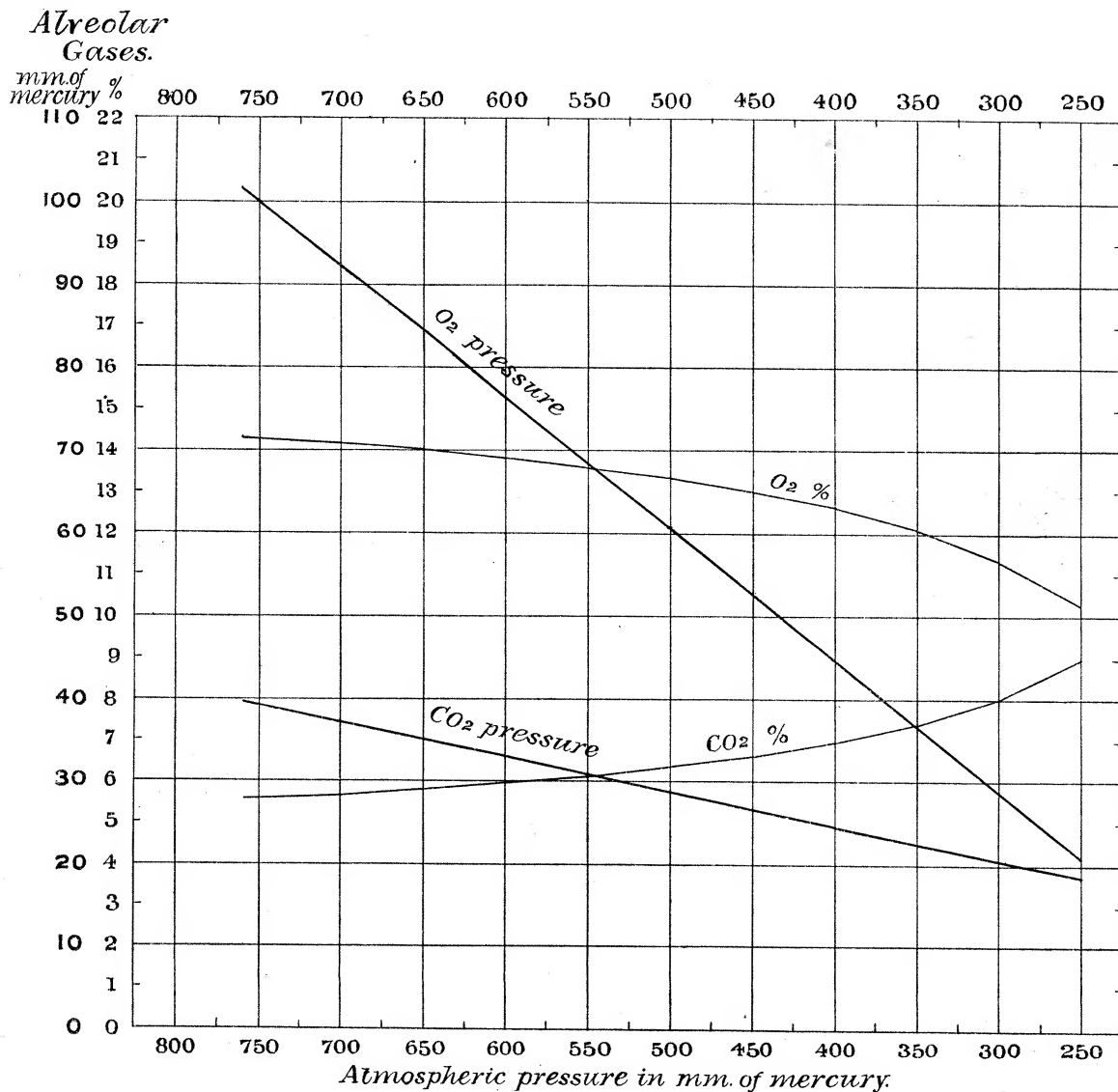


Chart II.

If the alveolar CO₂ values were known for points corresponding to pressures between 515 and 760 mm. of mercury, it is possible that a curve would replace the straight line which now represents the alveolar CO₂ pressure (Chart I), and that this curve would flatten as the normal barometric pressure for sea-level was approached, and in either case with increased air-pressure, then continue as a straight line parallel to the abscissæ, as it is known from the earlier experiments of HALDANE and PRIESTLEY,*

* 'Journ. Physiol.,' 1905, vol. 32, p. 225.

HILL and GREENWOOD,* and HALDANE and BOYCOTT,† that on short exposure to increased atmospheric pressure, even up to seven atmospheres in the case of GREENWOOD, the alveolar CO₂ pressure remained at normal value.

Broadly speaking, the percentage of hæmoglobin in the blood, both of men and women, increased progressively with the fall in barometric pressure, as is shown in Chart III, which represents graphically the hæmoglobin values given in Tables I and II.

Occasionally the mean value is seen to fall instead of to rise, or to be the same for two different altitudes. At each locality considerable variation was observed in the individual determinations. In the light of the knowledge of the diurnal variation in the percentage of hæmoglobin obtained by my colleagues on Pike's Peak,‡ some of the variations can be accounted for, as it was not possible to take the samples of blood of the different subjects at a corresponding time of day. From the values obtained it appears that for every 100 mm. fall of atmospheric pressure there is an average rise of about 10 per cent. in the hæmoglobin,§ and that this rise is about the same for women as for men. The individual variations in the increase are, however, very great. Considering, however, that among perfectly healthy individuals at normal atmospheric pressure HALDANE and LORRAIN SMITH|| and HALDANE,¶ working with accurate methods, found variations (mainly temporary) of as much as 13 per cent. on either side of the average, the individual variations at high altitudes are only such as might be expected.

It is possible that with increased atmospheric pressure the hæmoglobin would fall below 100 per cent., for the recent observations of Madame BORNSTEIN** on animals point to a decrease in the percentage of hæmoglobin as the atmospheric pressure increases.

Occasionally difficulty was experienced in making the hæmoglobin determinations, owing to the light, and at Ouray also a temporary fatigue affection of the eyes caused difficulty with some of the determinations, in consequence of which the mean value there recorded for women is probably higher than it actually should be.

In view of the work of WEBB, mentioned in an appendix to the Pike's Peak paper,†† on the increase in percentage of the mononuclear leucocytes in the blood of persons residing at high altitudes, blood films were made at every altitude. The results obtained may appear at a later date.

* 'Roy. Soc. Proc.,' 1906, vol. 70, p. 455.

† 'Journ. Physiol.,' 1908, vol. 37, Nos. 5, 6, p. 355.

‡ See preceding paper, 'Phil. Trans.,' B, vol. 203, p. 294.

§ The lines through the individual values plotted in Chart III would fit rather better if the increase of hæmoglobin percentage were taken as 9·5 for men and 10·5 for women for each 100 mm. fall of pressure. The data are not sufficient, however, to enable such fine distinctions to be drawn with any certainty.

|| 'Journ. Physiol.,' 1900, vol. 25, p. 340.

¶ *Ibid.*, 1901, vol. 26, p. 102.

** 'Pflüger's Archiv,' vol. 138, p. 609.

†† 'Phil. Trans.,' B, vol. 203, p. 312.

The diminution of the alveolar CO_2 pressure indicates an increase in the lung ventilation, whereby the alveolar oxygen pressure is maintained at a higher level.

Haemoglobin.

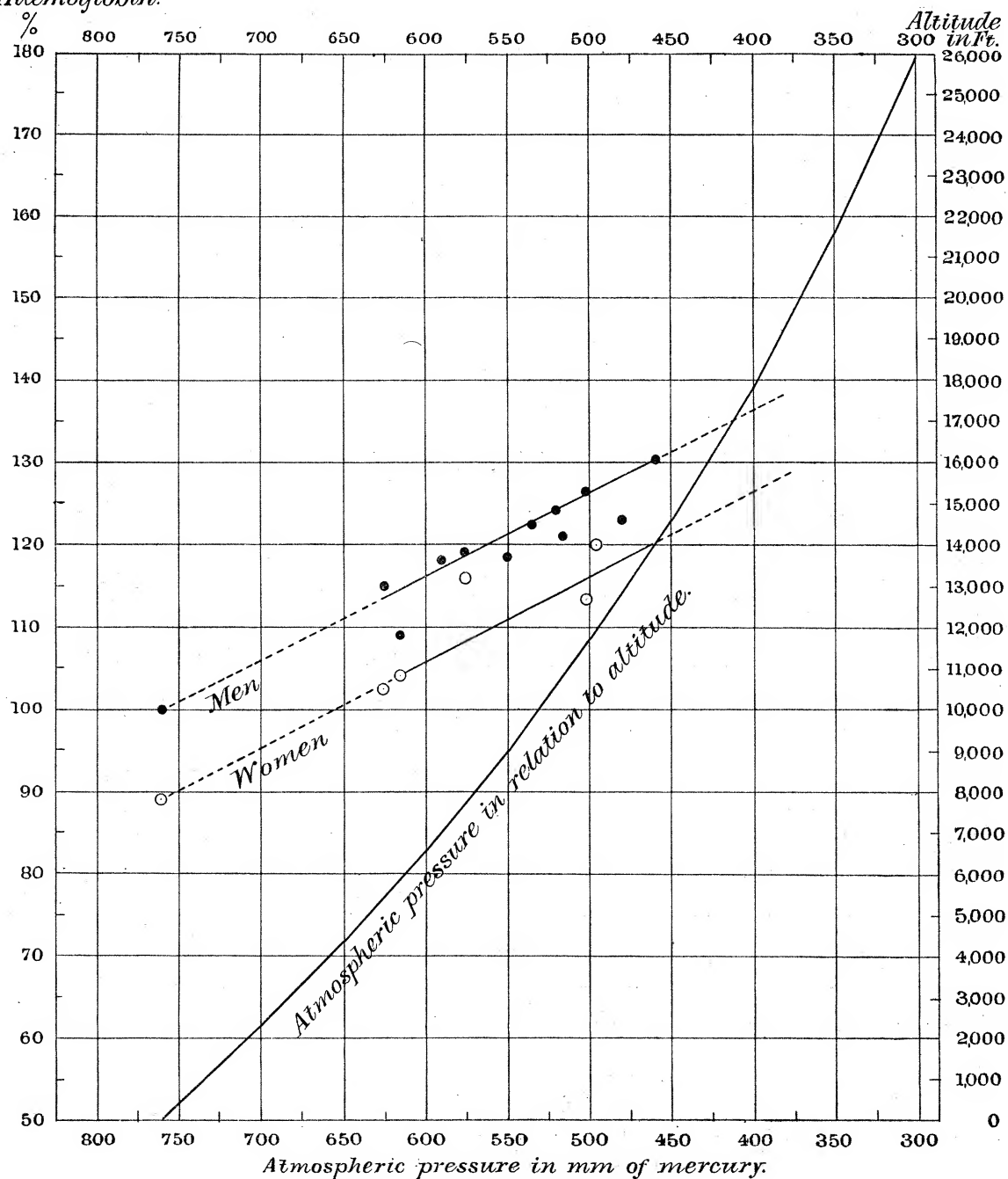


Chart III.

than would otherwise be the case; for the volume of air taken into the lung alveoli per unit mass of CO_2 produced is, of course, increased in inverse proportion to the relative diminution of the alveolar CO_2 pressure. An important consequence of this

is that each successive diminution of 100 mm. in atmospheric pressure causes a greater absolute increase in the lung ventilation. A drop of 100 mm. in barometric pressure from the pressure on Pike's Peak (458 mm.) would, for instance, cause nearly 60 per cent. greater increase in the lung ventilation than a drop of 100 mm. from the pressure at sea-level.

In their investigations in the steel chamber on the effects of reduced pressures on respiration BOYCOTT and HALDANE* found that on short exposure to want of oxygen the alveolar CO₂ pressure remained constant until the air pressure was reduced to about 550 mm. of mercury and the alveolar oxygen pressure to 62 mm. WARD has already shown the different effects produced by prolonged exposure to want of oxygen at high altitudes, but it is interesting to compare the steel chamber results with those obtained at corresponding pressures in Colorado. Whereas HALDANE and BOYCOTT's alveolar CO₂ was practically constant in short experiments down to a pressure of 550 mm., which corresponds to an altitude of nearly 9000 feet, we find that in acclimatised persons at Telluride, subjected under normal conditions to the same reduced pressure, the CO₂ pressure was only 30.1 mm., a fall of 23 per cent. of the normal.

To take another instance, with an artificially produced pressure of 350 mm., corresponding to an altitude over 20,000 feet, HALDANE's alveolar CO₂ was about 27.3, BOYCOTT's about 31.2. The value for HALDANE corresponds to the value now regarded as normal for a pressure of 458 mm.; and from the calculated curves in Chart II the CO₂ value for 350 mm. would be 22.4 mm. On the other hand, BOYCOTT's value at 350 mm. corresponds to an atmospheric pressure of between 550 and 600 mm. at an altitude of about 7000 feet. Thus in short exposures a much reduced pressure is required to produce the fall in the threshold exciting value of the CO₂ necessary for adaptation to a far higher pressure. Therefore even HALDANE, whose respiratory centre responded more promptly, was still at a physiological disadvantage, as he had 3.2 per cent. less oxygen in his alveolar air than he would have had at corresponding pressure after acclimatisation.

It is evident that, together with the rise in the percentage of hæmoglobin, the lowering of the alveolar CO₂ pressure is an important factor in the process of acclimatisation: for by this means the alveolar oxygen pressure is maintained at a higher value than would otherwise be the case at reduced atmospheric pressures. To take one or two examples: at the Camp Bird Mill, where the barometric pressure was reduced to 533 mm., the average of the alveolar CO₂ pressure was 29.9 and the hæmoglobin 122.6. From the dissociation curve given by DOUGLAS, HALDANE, and J. B. S. HALDANE,† it is seen that, even on the diffusion theory of the absorption of oxygen into the blood, the arterial blood at the corresponding oxygen pressure (66.1 mm.) would have been only 6 per cent. less saturated than normal; and that

* 'Journ. Physiol.,' 1908, vol. 37, p. 355.

† 'Journ. Physiol.,' 1912, vol. 44, No. 4, p. 283.

the arterial blood must, therefore, have contained at least 16 per cent. excess of oxygen. In spite of this the subjects were reacting to want of oxygen, as shown by the lowering of the alveolar CO_2 pressure and the rise in the percentage of hæmoglobin; this also shows that it is the partial pressure and not the actual amount of oxygen in the arterial blood that is the essential factor. Including Pike's Peak, as shown by my colleagues,* the arterial blood of residents at the various altitudes between 5000 and 14,000 feet must actually have been almost saturated to the normal extent. From earlier experiments of FITZGERALD† it is known that anæmic subjects, when at rest, have far less oxygen in their arterial blood than residents at high altitudes, for the hæmoglobin in such subjects may be reduced to one-third, and yet their alveolar CO_2 pressure is normal, or shows very little change.

If the alveolar CO_2 pressure at the Camp Bird Mill (altitude 9500 feet) had not been lowered, the alveolar oxygen pressure instead of being 66.1 would only have been about 53 mm. of mercury. Again at the Lewis Mine (altitude 12,500 feet) the oxygen pressure would have been only 42 mm. instead of 58 mm.

It is important to note that a very small difference in the oxygen pressure in the arterial blood has a great effect on the breathing and on the percentage quantity of hæmoglobin. In the preceding paper on the Pike's Peak Expedition, the process of acclimatisation is discussed in full, and the theory advanced that the diminution in the alveolar CO_2 pressure is produced by the alkalinity of the blood being diminished, the threshold exciting value of the CO_2 pressure depending upon the degree of alkalinity in the blood and the regulation of this by the kidneys. For further comment on this point readers are referred to the concluding section of the preceding paper.

From the calculated values in Chart III, persons subjected to a barometric pressure reduced to 312 mm., which pressure corresponds to the height reached by the DUC D'ABRUZZI,‡ the alveolar CO_2 pressure would be 21 mm. and the O_2 pressure 30 mm.; and on the assumption that the CO_2 pressure continues to fall at the same rate, the mountaineer who reached the summit of Mount Everest (altitude 29,000 feet) would only have a partial pressure of O_2 of about 24 mm. and 19 mm. of CO_2 .

With a view to ascertaining whether age or length of stay at high altitudes after one month had any influence on the alveolar CO_2 pressure, Tables V and VI have been prepared.

* See preceding paper, Section IV.

† 'Journ. Pathol.,' 1908, vol. 14, p. 328.

‡ 'Rivista del Club Alpino Italiano,' 1910, vol. 29.

TABLE V.

Number of subjects.	Age.	Alveolar CO ₂ pressure as recorded at different high altitudes.		
		Above mean.	Below mean.	Same as mean.
7	15-19	5	1	1
44	20-29	24	18	2
41	30-39	21	20	—
22	40-49	11	11	—
14	50-59	8	6	—
2	60-69	1	1	—
1	70-79	0	1	—
131		70	58	3

TABLE VI.

Number of subjects.	Length of time passed in high altitudes.	Alveolar CO ₂ pressure as recorded at different high altitudes.		
		Above mean.	Below mean.	Same as mean.
4	1-11 months	2	1	1
47	1-9 years	22	23	2
39	10-19 "	24	15	—
25	20-29 "	16	9	—
12	30-39 "	5	7	—
3	40-49 "	1	2	—
1	50-59 "	0	1	—
131		70	58	3

It will be seen from these tables that length of stay after the first month appears to have no distinct influence on the alveolar CO₂ pressure. There is perhaps some indication in Table V that in persons under 30 the fall in alveolar CO₂ pressure at high altitudes is less than at later age periods. It is not improbable that compensation by increased secretory activity of the lung epithelium is greater in young persons, so that there is less call for compensation by increased depth of breathing.

In general, no ill effects were observed in persons living at high altitudes, although the nervousness of the subjects, men and women alike, was very apparent. This condition was especially marked at altitudes of 7000 feet and upwards. The miners and others were fully conscious of their nervous tension, and attributed to this impulsive actions mentioned as common in mining communities at these altitudes.

The nervous effect of high altitudes was said by many to tell most heavily on the women and children. Too prolonged a stay at 10,000 feet and upwards was stated by some of the miners and others to become detrimental to health, and had in their own cases produced a desire to descend to lower levels; otherwise, life at high altitudes was generally considered beneficial to health.

Periodic nose-bleeding was recorded in one case at 10,000 feet. The different effects on the same person living at different places of the same altitude in Colorado were occasionally mentioned, and attributed to the different temperatures of such places. Except during great exertion, little mention was made of discomfort due to the altitude whilst at work, nor was the strain of working seven days in the week complained of physically by the miners, except in one or two instances when this strain had been kept up for a number of years. One subject (H. K.) experimented on at 10,300 feet, who had been engaged in construction work on the summit of Pike's Peak, said he had never felt discomfort whilst working at that altitude (14,100 feet), but had been obliged twice to change his gang of eight men during a period of a few weeks.

Another miner, at 10,090 feet, stated that he experienced no difficulty in playing a wind instrument. Two of the married women subjects, at 11,300 and 11,500 feet respectively, complained of ill-effects due to the altitude. One of these (F. W., 19), at 11,500 feet, found that the longer her stay the worse she became; the other (K. K., 26), in whom a slight degree of cyanosis was observable, complained, after 14 months' residence at 11,300 feet, of the continuance of attacks of palpitation of the heart, and of "die away" sensations, quite foreign to her at a low altitude.

A male subject (J. B.), who had spent from 8 to 11 years at an altitude of 11,300 feet without discomfort, stated that he felt a difficulty in breathing on going to a lower altitude, and that when spending a month at sea level (Los Angeles) 10 months previously, his fingers frequently became numb.

In the course of the investigation a number of observations were made on myself. In dealing with these, the results are tabulated in the order in which they were obtained, instead of at progressive altitudes (see Table VII). For comparison the mean values obtained for women residents at the same altitude are given in square brackets. It is thus possible to form an idea of the promptness of the physiological response shown by a non-inhabitant to conditions rapidly altering with regard to altitude.

Unless otherwise stated, values for the alveolar CO_2 pressure are not recorded till 24 hours had elapsed after arrival at a given altitude. The normal alveolar CO_2 pressure in M. P. F-G., at Oxford, is 34 mm. of mercury (barometric pressure 753 mm. of mercury). On leaving sea-level (New York), where the previous 18 months had been passed, two days were spent at an altitude of a few hundred feet, and the journey thence, of about 54 hours, was made direct to Colorado Springs (altitude 6000 feet).

No analysis apparatus was available for four days, by which time the alveolar CO_2 pressure had, owing to the fall of barometric pressure to 609 mm. of mercury, fallen to 32.3 mm. of mercury. The subsequent records, with some fluctuation in CO_2 pressure, showed a general tendency to diminish, and the mean value ultimately obtained for Colorado Springs was 31.3 mm. as against 30.45 mm. for women residents. Although these values are fairly close it must be remarked that the alveolar CO_2 in M. P. F-G. was not constant at the end of the first fortnight spent at Colorado Springs. This should be borne in mind, as subsequent records are based on a stay of from one to four days only, excepting at the Lewis Mine and on the summit of Pike's Peak, where the stay was less than eight hours. It must also be borne in mind that the alveolar CO_2 pressure of M. P. F-G. is 2.3 mm. lower at sea-level than the general average for women.

The slowness of the respiratory reaction, even when the change of altitude was great as well as abrupt, was fully apparent on Pike's Peak. Starting from Colorado Springs (6000 feet) to Manitou (7000 feet), the ascent of the mountain by train from the latter point was made without any sense of discomfort, but on arrival at the summit (14,100 feet) a slight degree of cyanosis was evident. The alveolar CO_2 determinations were made two hours after arrival, after a short walk on the summit. By this time the cyanosis had slightly increased and was accompanied by some unsteadiness of gait and slight aphasia. The alveolar CO_2 pressure, with a barometric pressure of 457 mm. of mercury, was 31.7 mm. of mercury, approximately the mean value at Colorado Springs, but slightly higher than the actual value obtained there on the previous day. The stay on the summit of Pike's Peak was about five hours; except for the symptoms previously mentioned, and a slight headache towards the end of the stay, it was unattended by discomfort. During the descent the headache increased continuously in severity, and was accompanied by a feeling of fulness in the head and nausea. By the time Colorado Springs was reached it became an effort to carry a light knapsack and overcoat, and owing to the increasing nausea it was necessary to lie down for a short time before going to the laboratory at Colorado College to make determinations on the alveolar air. The headache disappeared about two hours after the return to Colorado Springs, but an unusual sense of fatigue persisted till relieved by sleep. From the analyses it was found that four hours after leaving the summit of Pike's Peak the CO_2 pressure was 33.7 mm. of mercury, a higher value than was recorded at Colorado Springs under normal conditions. On the following day a normal value for the CO_2 pressure at Colorado Springs was obtained.

A later stay of the same duration on the summit of Pike's Peak, just after a stay of eight days at about 10,000 feet, did not produce similar discomfort, though more vigorous exercise was taken, but on this occasion it was not possible to make any alveolar air determinations. The process of acclimatisation is seen to be slow, as, though there was a fall in the partial pressure of CO_2 on going to Victor (altitude

9850 feet), the difference in CO_2 pressure as observed here and at Colorado Springs is not great and varies very little during the week spent at Victor, the Portland Mine and Mill (altitudes varying from 9850 feet to 10,300 feet). When compared, the mean value of CO_2 pressure in M. P. F-G. is definitely above that for women residents at the Portland Mine. With a decrease in altitude of 5000 feet at Denver, the next place visited, after a day's halt at Colorado Springs, the opposite effect is observed, for the CO_2 pressure only rose about 2 mm. This is explained by the already known tendency of the threshold exciting value of the CO_2 pressure to "lag" during a descent, so that on reaching a lower altitude the CO_2 values may bear more resemblance to those of the higher altitude lately left than to those of the lower altitude. Similar lagging was observed by WARD* on his descent from Monte Rosa to Zermatt and by BOYCOTT and HALDANE† in their long low pressure experiments in the steel chamber with WARD as the subject, and even in some of their shorter experiments.

Throughout the trip there is a general tendency for M. P. F-G.'s alveolar CO_2 percentage and pressure to be higher than that of the women residents, showing an incomplete adaptation and a slow response of the respiratory centre to want of oxygen. But by the end of the week spent in high altitudes the susceptibility of the respiratory centre had evidently increased, as at Telluride (altitude 8870 feet) and at the Lewis Mine (altitude 12,500 feet), the values for M. P. F-G. are approximately such as might be expected for women residents at those altitudes.

On the return to Colorado Springs two days after leaving Telluride—a journey involving great changes of altitude between 4000 and 11,000 feet—the same lagging of the alveolar CO_2 pressure was noticed during the first 24 hours, the CO_2 pressure being 29·7 mm. of mercury. Two days later the Colorado Springs value was again obtained. A still more noticeable instance of this "lagging" was observed on the return to sea-level (New York), where the alveolar CO_2 pressure averaged 30·9 mm. of mercury, considerably lower than the normal value (36 mm.) for M. P. F-G. at Oxford (200 feet above sea-level); and up to the time that, in accordance with an undertaking to the U.S. Customs authorities, the analysis apparatus had to be returned to England—10 days after leaving high altitudes, six spent at sea-level—the alveolar CO_2 pressure had not risen above 31·4 mm. of mercury, approximately the value for M. P. F-G. at Colorado Springs (6000 feet), where a final stay of two days had been made before departure from high altitudes to sea-level. This agrees with the results obtained by my colleagues on their return from high altitudes to sea-level (see preceding paper, Section V, p. 206).

The hæmoglobin percentage rose gradually during the stay in high altitudes. Fluctuating slightly from an initial value of 93 per cent. (an increase of 4 per cent. of the normal) at Colorado Springs, it reached 110 per cent. during the third week

* 'Journ. Physiol.,' 1908, vol. 37, Nos. 5-6, p. 386.

† 'Journ. Physiol.,' 1908, vol. 37, p. 367.

(Portland Mine, altitude 10,090 feet), fell with the lowered altitude at Denver and Ouray to 103 per cent., rose again at the Camp Bird Mine (altitude 11,300 feet) to 110 per cent., and reached its highest value, 112 per cent. (an increase of 23 per cent. of the normal), at Telluride (altitude 8,870 feet). Sixteen hours after the final return to Colorado Springs the hæmoglobin was still 111 per cent., and showed the same tendency as the CO_2 pressure to remain at high-altitude value, as on the sixth day after the return to sea-level (the tenth day after leaving high altitudes) it was still 108 per cent.

In conclusion, I wish to express my sincere appreciation of the kind help and cordial hospitality which I met with during the investigation, not only in the towns, but also in the remoter mining camps. To my colleagues in the expedition (Dr. HALDANE, Profs. YANDELL HENDERSON and SCHNEIDER, and Dr. DOUGLAS) I am indebted for much assistance, and for the loan of accurately standardised instruments. For a number of letters of introduction and other help, my thanks are specially due to President SLOCUM, of Colorado College, Mr. G. B. YOUNG, Mr. PECK, President of Portland Mine, and Mr. S. A. IONIDES, of Denver. My thanks are also due to the Council of the Royal Society for the grant (made to Dr. HALDANE) out of which my railway expenses were met.

Conclusions.

(1) In persons acclimatised at altitudes up to 14,000 feet the partial pressure of CO_2 in the air of the lung alveoli is invariably lower than at sea-level, so that the lung ventilation is correspondingly increased. The lowering of the CO_2 pressure is in direct proportion to the diminution of the barometric pressure, and amounts to about 4.2 mm. or 10.5 per cent. of the sea-level value for each 100 mm. of diminution of barometric pressure. The volume of air taken into the lung alveoli per unit mass of CO_2 produced is of course in inverse proportion to the *relative* diminution of the alveolar CO_2 pressure, consequently each successive diminution of 100 mm. in atmospheric pressure causes a greater *absolute* increase in the lung ventilation.

(2) In women, as at sea-level, the alveolar CO_2 pressure is about 3 mm. lower than in men.

(3) The effect of the increased lung ventilation is of course to diminish, to a very appreciable extent, the fall in the alveolar oxygen pressure and thus counteract the effects of want of oxygen.

(4) In acclimatised persons, for every 100 mm. fall of atmospheric pressure the percentage of hæmoglobin in the blood is increased by about 10 per cent. of the normal value for men at sea-level. As at sea-level, the values for women are about 11 per cent. lower than for men.

(5) In spite of the diminished alveolar oxygen pressure and consequent slightly reduced percentage saturation with oxygen of the arterial hæmoglobin, the arterial blood contains considerably more oxygen at high altitudes than at sea-level. The

symptoms of oxygen deficiency at high altitudes are therefore due to deficiency, not in the *amount*, but in the *partial pressure* of oxygen in the arterial blood.

(6) The acclimatisation changes take a considerable time both to develop and to pass off. •

Graphic representations and tables are given of the alveolar gas pressures and hæmoglobin percentage in acclimatised persons at varying atmospheric pressures and heights above sea-level.
